

Faculty Scholarship

---

6-7-2022

## Respiratory Morbidity and Neurodevelopmental Outcomes in Infants Born Preterm: A Complex Web

Anna Maria Hibbs  
*Case Western Reserve University*, [annamaria.hibbs@case.edu](mailto:annamaria.hibbs@case.edu)

Author(s) ORCID Identifier: [Anna Maria Hibbs](#)

Follow this and additional works at: <https://commons.case.edu/facultyworks>

Digital part of the [Developmental Neuroscience Commons](#), and the [Pediatrics Commons](#)  
Commons

---

### Network Recommended Citation

Hibbs, A.M. (2022), Respiratory morbidity and neurodevelopmental outcomes in infants born preterm: A complex web. *Dev Med Child Neurol*, 64: 1185-1185. <https://doi.org/10.1111/dmcn.15295>

This Letter to the Editor is brought to you for free and open access by Scholarly Commons @ Case Western Reserve University. It has been accepted for inclusion in Faculty Scholarship by an authorized administrator of Scholarly Commons @ Case Western Reserve University. For more information, please contact [digitalcommons@case.edu](mailto:digitalcommons@case.edu).

CWRU authors have made this work freely available. [Please tell us](#) how this access has benefited or impacted you!

- Ebrahimi-Fakhari D, Stires G, Hahn E, Krueger D, Franz DN. Prenatal Sirolimus Treatment for Rhabdomyomas in Tuberous Sclerosis. *Pediatr Neurol* 2021; 125: 26–31.
- Capal JK, Bernardino-Cuesta B, Horn PS et al. Influence of seizures on early development in tuberous sclerosis complex. *Epilepsy Behav* 2017; 70: 245–52.
- Kotulska K, Kwiatkowski DJ, Curatolo P, et al. Prevention of Epilepsy in Infants with Tuberous Sclerosis Complex in the EPISTOP Trial. *Ann Neurol* 2021; 89: 304–14.
- Wilkie AO. Cancer drugs to treat birth defects. *Nat Genet* 2007; 39: 1057–9.

Received: 9 May 2022 | Accepted: 10 May 2022

DOI: 10.1111/dmcn.15295

## Respiratory morbidity and neurodevelopmental outcomes in infants born preterm: A complex web

Anna Maria Hibbs 

UH Rainbow Babies & Children – Paediatrics, Cleveland, OH, USA

Yu et al. report the identification of distinct early-life longitudinal trajectories of respiratory support that are associated with neurodevelopmental outcomes in infants born preterm.<sup>1</sup> The most widely used marker of respiratory status in the neonatal intensive care unit (NICU), bronchopulmonary dysplasia, is known to correlate with long-term neurodevelopmental outcomes.<sup>2</sup> This study enriches prior work linking respiratory status in the NICU with neurological outcome by incorporating detailed early-life longitudinal data, as well as by using objective clustering analyses, as opposed to expert opinion, to identify distinct groups.

The causal pathways underpinning the relationship between respiratory support in the NICU and neurodevelopmental outcomes are likely to be complex.<sup>3</sup> One possibility is simply that respiratory status acts as a marker of severity of illness, either cross-sectionally or longitudinally, and that its link with neurodevelopment is not of a directly causal nature. A second possibility is that pulmonary and neurological morbidity share common causal antecedents, such as infection, inflammation, or microbiome alterations. Preterm birth itself is of course the most significant common antecedent for both pulmonary and neurological morbidity. Third, pulmonary disease, and the interventions we use to support it, may trigger biological mechanisms that directly contribute to neurological injury. Possible mechanisms could include, but are not limited to, inflammation, intermittent hypoxia, and altered early-life human interactions.<sup>2,4</sup> However, it is probable that all three types of potential causal relationships between respiratory disease and neurological morbidity are at play. The lung-brain axis in infants born preterm is likely a complex web rather than a straightforward pathway.

The current findings reported by Yu et al. identify infants at high risk for neurodevelopmental impairment by 8 weeks of age, based on clinical variables and respiratory trajectory.<sup>1</sup> This risk stratification could facilitate targeted referrals for intensive neurodevelopmental monitoring and intervention, as well as selection of infants for trials of novel interventions. Future research directions could include identification of biomarkers associated with each respiratory trajectory, which could further elucidate the biological mechanisms underlying the associations of the trajectories with neurodevelopmental impairment.

### DATA AVAILABILITY STATEMENT

Not required

### ORCID

Anna Maria Hibbs  <https://orcid.org/0000-0001-6773-068X>

### REFERENCES

- Yu W-H, Chu C-H, Lin Y-C, et al. Early-life respiratory trajectories and neurodevelopmental outcomes in infants born very and extremely preterm: A retrospective study. *Dev Med Child Neurol* 2022; 64: 1246–53.
- Sriram S, Schreiber M, Msall M, et al. Cognitive development and quality of life associated with BPD in 10-year-olds born preterm. *Pediatrics* 2018;141:e20172719.
- Gagliardi L, Bellù R, Zanini R, Dammann O. Bronchopulmonary dysplasia and brain white matter damage in the preterm infant: a complex relationship. *Pediatr Perinat Epidemiol* 2009;23:582–90.
- Di Fiore JM, Raffay TM. The relationship between intermittent hypoxemia events and outcomes in neonates. *Exp Neurol* 2021;342:113753. <https://doi.org/10.1016/j.expneurol.2021.113753>

This commentary is on the original article by Yu et al. on pages 1246–1253 of this issue.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2022 The Author. *Developmental Medicine & Child Neurology* published by John Wiley & Sons Ltd on behalf of Mac Keith Press.